Remarks

Claims 1 and 2 are pending after the entry of new claim 2. Claim 1 is amended and new claim 2 is submitted with support in the original claim language and throughout the specification, particularly at page 6, lines 9-11. The specification is amended to provide the current status of the parent application and to correct inadvertent typographical errors. An amended Abstract is also provided as required. It is believed that these amendments and new claim add no new matter. In light of these amendments applicants respectfully request reconsideration of this application, entry of these amendments and new claims, and allowance of the application to issue.

Rejection Under 35 U.S.C § 103

Claim 7 is rejected as allegedly obvious over Honard et al. in view of Georgaddze et al.

With respect to the obviousness rejection over Honard et al. US 4,685,900 in view of Georgadze et al. it is stated that Honard et al. discloses a plasmapheresis device and method for treating any disease by removal of noxious substances or cells from the blood. In the view of the examiner the method comprises withdrawing blood from a patient, treating said blood by plasmapheresis and returning the treated blood to the patient. It is stated that antibodies to islet cells may be used to treat diabetes mellitus. The examiner acknowledges that Honard does not expressly disclose that the treatment is for treating the diabetic ischemia of a foot.

With respect to the Georgadze et al. the examiner points out that this document describes plasmapheresis treatment which may be used for the treatment of ischemia in the lower

extremities of diabetics. In the view of the examiner the reference discloses that the plasmapheresis corrects the biochemical and coagulation parameters of the blood and thereby preserves the extremity from amputation in most patients.

The examiner concludes that with respect to the treatment of the foot it would have been obvious for persons skilled in the art based on the teaching of Georgadze to use plasmapheresis as treatment for persons diagnosed with diabetic ischemia of the foot since the foot is obviously lower extremity. According to the Examiner, such treatment would be beneficial to preserve the foot from amputation.

Applicants first note that the present application was filed with a single claim, claim 1. Thus, the reference in the Office Action to claim 7 is treated herein as reference to claim 1.

Applicants have amended claim 1 by introducing the feature that by the claimed method of treatment high molecular weight proteins are removed from the blood. The recitation of this feature illustrates a non-obvious distinction over the cited Georgazde et al. and Honard et al. references.

Honard et al. does not suggest each and every element of claim 1 in the present application. More specifically, Honard et al. teaches that a wide variety of diseases including diabetes mellitus can be treated by using specific biologicals to treat specific diseases. For the case of diabetes mellitus Honard et al. proposes using biological ligands to bind and remove circulating antibodies to islet cells from a patient's blood to treat the disease. Furthermore, the reference does not mention treating diabetic ischemia of a foot in a patient diagnosed with

diabetic ischemia of a foot. This is in contrast to the present method, which uses the selective removal of large molecular weight proteins to treat the specific disease of diabetic ischemia of a foot. The focus of Honard is on the function of the specific biological, and the presence and use of the specific biological is carried through in the description of the device and process. It is the use of the specific biological that provides the advantage claimed by Honard et al. There is no suggestion that removing high molecular weight proteins will provide any beneficial effect. Thus, there is no suggestion in Honard et al. that a method like that claimed would be effective to treat any disease, much less diabetic ischemia of a foot.

With respect to the reference Georgadze et al., which was cited as an English abstract, we submit herewith the complete English translation of the reference (attached as Exhibit 1). The reference relates to the use of plasmapheresis in the treatment of critical degrees of ischemia in diabetic and angiopathies of lower extremities. The reference teaches the application of gravitation plasmapheresis for the treatment of critical stages of ischemia of the lower extremities in patients with diabetes mellitus (see 1st page, 2nd paragraph of English translation). According to page 1, 2nd paragraph using the gravitation plasmapheresis leads to a fractionation of the blood which is haemorheologically oriented and adds to the extraction of bacterial toxins, paraproteins, CIC, killer cells etc.

The reference does not contain further information about the used material for the plasmapheresis and the used system or the eliminated components of the blood. Thus, it does not expressly suggest the selective removal of large molecular weight proteins. Furthermore, it can

be concluded from the first page 2nd paragraph that the centrifugation plasmapheresis technique described in the Georgazde et al. document leads to the non-selective elimination of numerous types of blood components that can contribute to diabetic ischemia. This procedure is, by its very nature, non-selective. Thus there is no implicit suggestion in Georgadze et al. to selectively remove large molecular weight proteins. In contrast, the treatment according to the invention selectively removes high molecular weight proteins and preferably low density lipoprotein, cholesterol, alpha-2-macroglobulin and similar high molecular weight proteins.

Furthermore the reference teaches that a medicament Rheopolyglukin was used as an infusion substance (see page 2, 2nd paragraph of English translation). Such a medicament is not used in the treatment according to the present invention. While this component of the Georgadze et al. method is not stated in the reference to be required for success, it is unpredictable that the method would work without this component. Thus, because the reference used Rheopolyglukin, and suggests its future use (see page 5, item 2 of the Conclusions), the reference does not suggest a method in which it is not used. Since the method of the invention does use this component, the invention is not suggested by the reference.

Therefore the present invention uses method steps that differ from and are not suggested by Georgazde et al., namely, that specific high molecular weight proteins are removed from the blood of the patient. After that the blood is reinfused into the patient and thereby the diabetic ischemia of the foot is treated. Georgadze et al. has the disadvantage of being less selective than the present invention. As explained above the treatment according to the invention is very

selective compared to the gravitational plasmapheresis treatment according to the Georgazde et al. reference.

The conclusion of the in the office action that it was obvious for persons skilled in the art based on the teaching of Georgazde et al. to use plasmapheresis as treatment for persons diagnosed with diabetic ischemia of the foot is wrong for the present claim because Georgazde et al. discloses a totally different plasmapheresis procedure compared to the claimed invention. This procedure, like the procedure described in Honard et al., discloses a technique in which toxic substances are removed from the blood, but not by the selective removal of large molecular weight protein components of the blood. Thus neither reference discloses or suggests the aspect of the claimed invention that is missing from the other reference. Because the references taken alone or together do not suggest the selective removal step of the present invention, the invention of claims 1 and 2 is not obvious over the art.

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Respectfully submitted,

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